IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant(s): Gleave, et al. Application No.: 10/646,436 Filed: 8/21/2003 Title: RNAi Probes Targeting Cancer-Related Proteins Attorney Docket No.: UBC.P-030	Group Art Unit: 1635 Examiner: Kimberly Chong Confirmation No. 9171

BRIEF FOR APPELLANT

This brief is filed in support of Applicants' Appeal from the final rejection mailed 1/9/2006. Consideration of the application and reversal of the rejections are respectfully urged.

Real Party in Interest

The real party in interest is The University of British Columbia.

Related Appeals and Interferences

To Applicants' knowledge, there are no related Appeals or interferences.

Status of Claims

Claims 1-4, 10-14, 20-23, 29, and 34 are pending in this application. Claims 5-9, 15-19 22, 24-28 and 30 have been canceled. Claims 1-3 and 10-13 are rejected and are the subject of this appeal. Claims 4 and 14 are objected to as containing non-elected subject matter, while claims 31 and 33 are objected to as being dependent on a rejected claim. Claims 20, 21, 23, 29, 32 and 34 are withdrawn.

Status of Amendments

The amendment after final filed on February 16, 2006 has been entered. The amendment after final filed on March 23, 2006 has not been entered.

Summary of Claimed Subject Matter

The claimed invention relates to RNA molecule having a sequence effective to mediate degradation or block translation of mRNA that is the transcriptional product of a target gene, wherein the target gene encodes clusterin, and the RNA molecule comprises a sequence of bases complementary to the gene for human clusterin. (Claim 1). As explained in the specification,

> Within any given mRNA molecule, there are sites which are affected by RNAi probes, and sites which are not. Thus, one cannot simply chop up the overall sequence into subsequences of appropriate lengths (for example, 21 to 23 base pairs) to arrive at functional RNAi-based therapeutics.

(Specification, Page 1) The present application discloses multiple RNA sequences that are shown to be effective for this purpose, including SEQ ID NOs: 1-16. (Table 1, Page 7, Examples 7-20, Figs. 7-19)

As explained in the specification on Page 6,

> clusterin is expressed in increased amounts by prostate tumor cells following androgen withdrawal. Furthermore, it has been determined that antisense therapy which reduces the expression of clusterin provides therapeutic benefits in the treatment of cancer. In particular, such antisense therapy can be applied in treatment of prostate cancer and renal cell cancer. (PCT Patent Publication WO 00/49937, which is incorporated herein by reference). Administration of therapeutic agents clusterin also can enhance sensitivity of cancer cells to chemotherapeutic agents and to radiotherapy both *in vitro* and *in vivo*.

Thus, the sequence that are the subject of the claims invention can be used alone or in combination with other chemotherapy agents or apoptosis inducing treatment concepts in the treatment of prostate cancer, sarcomas such as osteosarcoma, renal cell carcinoma, breast cancer, bladder cancer, lung cancer, colon cancer, ovarian cancer, anaplastic large cell lymphoma and melanoma.. (Page 6) In addition, clusterin has been shown to promote amyloid plaque

formation and to be critical for neuritic toxicity in mouse models for Alzheimer's disease. Thus, the sequences of the invention can also be used in the treatment of Alzheimer's disease. (Pages 6-7).

Grounds of Rejection to be reviewed on Appeal

Claims 1-3 and 10-13 are rejected as anticipated by US Patent No. 6,383,808.

Argument

Claims 1-3 and 10-13 stand rejected as anticipated by US Patent No. 6,383,808 of Monia. Claims 31 and 33 which specifically recite the elected sequence (SEQ ID NO: 10) are indicated as allowable.[1]

The Monia reference relates primarily to antisense compositions that inhibit clusterin expression, and a multiplicity of DNA sequences are disclosed. The entire disclosure of the Monia patent concerning RNA oligonucleotides as inhibitors is a single passage in Col. 6, that reads:

> In the context of this invention, the term "oligonucleotide" refers to an oligomer or polymer of ribonucleic acid (RNA) or deoxyribonucleic acid (DNA) or mimetics thereof. ... Antisense compounds include ribozymes, external guide sequence (EGS) oligonucleotides (oligozymes), and other short catalytic RNAs or catalytic oligonucleotides which hybridize to the target nucleic acid and modulate its expression.

Monia does not disclose even one actual RNA sequence. Applicants submit that Monia does provide an enabling disclosure of any species within the scope of the invention as claimed, and therefore that the reference is not properly relied on as anticipatory of the claimed invention.

---

[1] Claims 4 and 14 are objected to because they recite additional sequences beyond SEQ ID NO: 10, and the Examiner asserts that these are separate inventions and that it would pose an undue burden to search more than one sequence. Claims 1-3 and 10-13 are generic, and therefore would constitute linking claims were they found to be allowable, necessitating the consideration of the remaining sequences.

"Prior art under §102(b) must sufficiently describe a claimed invention to have placed the public in possession of that invention." *In re Elsner*, 72 USPQ2d 1038, 1041 (Fed. Cir. 2004). "Such possession is effected if one of ordinary skill in the art could have combined the publication's description of the invention with his own knowledge to make the claimed invention." *In re Donohue*, 226 USPQ 619, 621 (Fed. Cir, 1985). Applicants submit that this combination of knowledge must not require invention or the type of experimentation that would be considered "undue" under the enablement standard if a reference is to be considered enabling. Indeed, as noted in the MPEP § 2121.01,

> "the disclosure in an assertedly anticipating reference must provide an enabling disclosure of the desired subject matter; mere naming or description of the subject matter is insufficient, if it cannot be produced without undue experimentation. *Elan Pharm., Inc. v. Mayo Found. For Med. Educ. & Research*, 346 F.3d 1051, 1054, 68 USPQ2d 1373, 1376 (Fed. Cir. 2003).

The *Elan* case cited in the MPEP is relevant to and parallels the facts in that case. The claim at issue in *Elan* was one directed to a transgenic rodent having a certain expressed transgene. The allegedly anticipatory prior art was an issued US Patent that contained a generic statement that is provided a non-human transgenic animal that expressed the same transgene. The referenced patent did not disclose an actual transgenic animal but instead contained a catalog of how to make such an animal. After noting that the patentee, Elan, had argued that the reference did not indicate which of the method and vectors might reasonably be expected to succeed in producing the mouse, the Federal Circuit remanded the case to the District Court for a determination on whether the disclosure of the reference was sufficient for enablement. 68 USPQ 2d at 1375-1376.

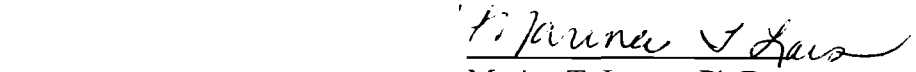
In the present case, all the Monia patent provides is a generic mention of RNA molecules as an alternative to the DNA species disclosed, and an invitation to experiment to find ones that may work. There is no disclosure of even one RNA sequence, and thus the reference does not place the public in possession of any embodiment within the scope of the presently claimed invention.

In the Advisory Action of March 2, 2006, the Examiner states that the argument that Monia does not disclose a single RNA species is not persuasive because "Applicant has not provided a reason why Monia et al. is not enabling." Applicants submit that the complete absence of even a single example is in itself evidence of lack of enablement that the Examiner has failed to respond to in any substantive way.

Further, the Examiner states that the argument is not persuasive because "there is no evidence of record that shows why the RNA oligonucleotides targeted to clusterin as disclosed by Monia et al. do not mediate degradation or block translation of clusterin mRNA." This statement is an amazing logical fallacy. Quite evidently, some RNA oligonucleotides do achieve this result, but they are disclosed **only** in Applicants' specification. There are no RNA oligonucleotides disclosed in Monia that could be specifically addressed to say whether or not they were actually operable, so it is not apparent how Applicants would present the evidence the Examiner asserts is lacking. Moreover, the uncontroverted statement in the specification is that not all RNA oligonucleotides are effective. This is the point of Applicants' argument, and the Examiner has not explained how the mere statement that RNA species may also exist can be considered an enabling disclosure of those species sufficient for a conclusion of anticipation.

In view of the foregoing, Applicants submit that the anticipation rejection of claims 1-3 and 10-13 should be reversed.

Respectfully submitted,



Marina T. Larson Ph.D.
PTO Reg. No. 32,038
Attorney for Applicant
(970) 262 1800

Claims Appendix

1. An RNA molecule having a sequence effective to mediate degradation or block translation of mRNA that is the transcriptional product of a target gene, wherein the target gene encodes clusterin, and the RNA molecule comprises a sequence of bases complementary to the gene for human clusterin.

2. The RNA molecule of claim 1, wherein the sequence of bases complementary to the gene encoding human clusterin has a length of 19 to 21 nucleotides.

3. The RNA molecule of claim 2, wherein the sequence of bases complementary to the gene encoding human clusterin has a length of 19 nucleotides.

10. A pharmaceutical composition comprising an RNA molecule having a length of less than 49 bases and having a sequence effective to mediate degradation or block translation of mRNA that is the transcriptional product of a target gene, wherein the target gene encodes clusterin, and the RNA molecule comprises a sequence of bases complementary to the gene for human clusterin, together with a pharmaceutically acceptable carrier.

11. The pharmaceutical composition of claim 10, wherein the pharmaceutically acceptable carrier is a sterile injectable solution.

12. The pharmaceutical composition of claim 11, wherein the sequence of bases complementary to the gene encoding human clusterin has a length of 19 to 21 nucleotides.

13. The pharmaceutical composition of claim 12, wherein the sequence of bases complementary to the gene encoding human clusterin has a length of 19 nucleotides.

Evidence Appendix

none

Related Proceedings Appendix

none